

**REMARKS/ARGUMENTS**

These amendments and arguments are submitted in response to the Office Action dated March 22, 2004. The telephone interview of April 26, 2004 of the undersigned with examiner Yoon is acknowledged with appreciation. In that interview some possible amendments to claim 1 to further distinguish the invention from Alpenfels et al. were discussed. One such amendment is made herein; if the examiner considers other language to be more appropriate, he is encouraged to telephone the undersigned.

The invention claimed in this application is a process for casting a polyacrylamide gel that enables such a gel to be cast in a plastic gel enclosure, e.g., between plastic plates. As pointed out in the specification, there is a problem associated with the use of plastic plates or enclosures for such gels, namely that oxygen - which may be present in the plastic or which may seep through it (as air) - causes irregularities in the gel pore size near the gel/plastic interface, which in turn produce a distortion of the solute bands in the gel. As discussed in earlier communications, such problems do not occur when casting gels between glass plates since glass is impermeable to gases.

Applicant's solution to this problem is the incorporation in the gel casting mixture (including an acrylamide and a cross-linking agent) of an oxygen scavenger selected from the group consisting of sodium sulfite, sodium bisulfite, sodium thiosulfate, sodium lignosulfate, ammonium bisulfite, hydroquinone, diethylhydroxyethanol, diethylhydroxylamine, methylethylketoxime, ascorbic acid, erythorbic acid, and sodium erythorbate. This makes it possible to take advantage of the benefits of using plastic plates or other enclosures while at the same time being able to provide a gel that functions with similar accuracy to one enclosed within glass plates. With one exception (Alpenfels et al.), the cited prior art is clueless as to how to accomplish this, and that exception discloses a totally different technique.

Claims 10-13 were rejected under 35 U.S.C. 112, first paragraph, for lack of enabling disclosure as written. Applicant agrees that the claims contained an erroneous quantity, and have amended them in accordance with the suggestion in the Office Action. No new matter has been

added thereby. Claim 9 is also amended to correct a typographical error in the spelling of "styrene".

There being no art rejection of claims 10-13, Applicant requests that they be indicated as allowable in the next communication.

\ Claims 1-3 and 6-9 stand rejected as obvious over the combination of Hochstrasser et al. with Alpenfels et al. or Lau et al.

Claim 1 has been amended to state that the inventive process (involving the polymerization of the mixture of monomers) is conducted in an uncoated plastic gel enclosure (for instance, between uncoated plastic plates). This amendment was discussed with the examiner on April 26, with the examiner agreeing that this limitation is supported by the statement in the specification in example 3 (page 5 line 21) that the example was conducted in uncoated plastic plates.

The term "uncoated plastic gel enclosure" is meant to refer to plastic enclosures that lack an oxygen barrier coating, for example, a barrier such as disclosed in Alpenfels et al.

Hochstrasser et al. disclose a process for gel formation in which the gel is to be used as a matrix in a process for detection of biological material by silver staining. The focus in this reference is on the reduction of background staining of the gel. According to the Hochstrasser et al. invention, sodium thiosulfate was found suitable for this purpose, and is therefore included in their gel formation process. As discussed previously, there is no suggestion in Hochstrasser et al. or elsewhere that thiosulfate could also reduce the occurrence of irregularities at the interface between a gel and a plastic enclosure caused by the presence of oxygen.

Background staining occurs in the bulk of the gel after the gel has been removed from the enclosure and stained, while interfacial irregularities, which is the issue involved in the present invention, occur at the interface between the gel and the enclosure while the gel is being cast. One would not readily suspect that an additive such as thiosulfate that is known only to serve its function in the bulk of the gel would be effective in correcting problems that arise only at the gel-enclosure interface.

The citation of Hochstrasser et al. by the examiner fails to consider the Hochstrasser et al. disclosure as a whole, as is required by 35 USC 103. Hochstrasser et al. sought to deal with a

specific problem - reduction or elimination of undesirable background staining. In their work, these inventors tried a number of compounds for this purpose, but found that only one - sodium thiosulfate - accomplished it. On the other hand, they tried other compounds within the scope of the present claims, and found that these were detrimental to their process. As pointed out in the previous communication Hochstrasser et al. state that only sodium thiosulfate produced good results in their experimentation, but that sodium sulfite, sodium bisulfite, sodium hydrosulfite, potassium metabisulfite, sodium sulfate, and others produced undesirable results (col. 10 lines 25-68; table bridging cols. 13 and 14).

Hochstrasser et al. thus contains teachings that teach both towards and away from the claimed invention. That is, Hochstrasser et al. teach that sodium thiosulfate should be incorporated in the gel formation process, but that, on the other hand, sodium sulfite and bisulfite (both claimed for Applicant's process) should not be incorporated. It is inappropriate for the examiner to rely only on information that supports one point of view while not taking into account information that explicitly directs those skilled in the art to not use compounds claimed by Applicant. Panduit Co. v. Dennison Mfg. Co., 227 USPQ 337 (Fed. Cir. 1985); Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocure, Inc., 230 USPQ 416 (Fed. Cir. 1986).

Applicant notes that the examiner implicitly recognized these contrary teachings inasmuch as claims 4 and 5 are not rejected over this combination of references.

The overall Hochstrasser et al. disclosure does not render Applicant's claimed process obvious, whether alone or in combination with the secondary references. In addition, those skilled in the art would obtain no information from Hochstrasser et al. on solving the problems caused by oxygen at the surface of the gel.

Hochstrasser et al. ran their process in glass plates only. Consequently, there were no problems caused by oxygen. Accordingly, the examiner cites Alpenfels et al. and Lau et al. for the proposition that advantages of plastic plates are known and that it would be obvious to run the Hochstrasser et al. process in plastic plates. Applicant agrees that plastic and glass plates were known at the time his invention was made. However, as mentioned, Hochstrasser et al. does not, and did not need to, deal with the problems of oxygen contact with the gel that are encountered when using plastic plates.

Alpenfels et al., on the other hand, were aware that oxygen diffusion into the gel should be prevented (though the nature of the problem caused is not mentioned in this reference). They dealt with this by the use of plastic films that had a special coating that provided an oxygen barrier. This is described in Alpenfels et al. at col. 5 lines 30-45. This use of plastic plates or films having an oxygen barrier obviates the need for use of Applicant's oxygen scavengers. On the other hand, the use of Applicant's oxygen scavengers removes the need for an oxygen barrier, which can decrease the production cost.

Thus, those skilled in the art would not find it obvious to combine the Hochstrasser et al. process with that of Alpenfels et al. in order to avoid the problems associated with the presence of oxygen since the latter already provides a means for dealing with that. Additionally, those skilled in the art would be taught away from using certain of the claimed salts by Hochstrasser et al. Finally, any combination of the two references would result in the Hochstrasser et al. process being carried out using the Alpenfels specially constructed plastic films with oxygen barriers, whereas Applicant's invention excludes the use of such barriers.

In the interview of April 26, the examiner commented that Alpenfels et al. teach only that the use of an oxygen barrier coating is preferred, so that Alpenfels et al. could be considered to teach that their process could be conducted without a coating. Applicant agrees that Alpenfels et al. states that the plastic plates are "preferably" coated with an oxygen barrier (col. 5 lines 30-45). However, Alpenfels et al. do not contain any effective disclosure or guidance of how to operate a gel polymerization process in plastic enclosures in any way other than using an oxygen barrier coating. With the express need in Alpenfels et al. for a coating to serve as an oxygen barrier and no guidance to indicate how else the process might be run or when such a coating might not be needed, those skilled in the art would not consider operating the Alpenfels process in plastic enclosures in any way other than with the use of some type of oxygen barrier.

Applicant thus submits that claims 1-3 and 6-9 are not rendered obvious from the combined disclosures of Hochstrasser et al. and Alpenfels et al.

Lau et al. deal with aspects of the construction of a system of plates for use in gel production. In passing they mention (col. 4 lines 38-43) that the system could include either glass or plastic plates. The reference discloses nothing further about plastic plates. It does not

disclose whether or not their plastic plates present any problem with oxygen contact at the gel surface or gel-plastic interface. In the absence of any information to the contrary, one can only assume that if anyone skilled in the art were in fact to use plastic plates in a Lau et al. type of construction, they would provide the plates with an oxygen barrier as disclosed in Alpenfels et al. to avoid this problem, or they would encounter this problem. In that connection, Applicant notes that Ogawa et al. previously cited, specifically disclose that a gel-forming solution should be sealed from oxygen contact (col. 1 line 63 - col. 2 line 7). However, in that reference, the sealing was accomplished with the use of glass plates.

Applicant's claimed process provides cross-linked polyacrylamide gels of good quality contained within plastic plates or other enclosures. The prior art (except possibly for Alpenfels et al.) simply does not provide such a product, nor does it render it obvious how such a product may be obtained.

For the above reasons, the rejection of claims as obvious over the proposed combination of Hochstrasser et al with either Alpenfels et al. or Lau et al. is not appropriate and in any event the cited art in combination does not render the claims obvious. Applicant requests that this rejection be withdrawn.

Claims 1-9 are again rejected as being obvious over the combination of Alpenfels et al. with Saunders et al. or Flesher et al. Here the examiner recognizes that Alpenfels et al. does not involve the inclusion of any compound that is an oxygen scavenger, and proposes to combine this reference with the latter two. However, this combination is not appropriate.

The process of Alpenfels et al., taken as a whole, is designed for the purpose of producing cross-linked polyacrylamide electrophoresis gels for separation of materials such as proteins. The examples show use of ammonium persulfate (APS) with TEMED as a polymerization catalyst.

Saunders et al., on the other hand, disclose a process for producing linear polymers of polyacrylamide in which the amount of cross-linking is kept to a minimum (col. 1 lines 8-9). Cross-linking is said to be undesirable because such products are water-insoluble (col. 1 lines 51-54). The Saunders et al. products must be water-soluble; they are used not for electrophoresis



but as flocculants for suspended solids in water and strengthening agents for paper. Saunders et al. is directed to an improvement in the catalysts previously used for producing such products.

The examiner takes the position that it would be obvious to combine the two disclosures because the use of the redox polymerization catalysts involves basic polymerization chemistry, irrespective of the end use of the products, and that cross-linking is known to be mainly dependent on the amount of cross-linking monomer used, and not on the nature of the catalyst.

However, Applicant submits that while both references involve acrylamide polymerization, the issue of whether they may be combined cannot be reduced to one of "basic polymerization chemistry". The two patents produce different products - one (Alpenfels et al.) is aimed at producing a cross-linked polymer (and includes a cross-linking agent), the other (Saunders et al.) at producing a linear polymer with as little cross-linking as possible. The products have totally different properties and are aimed at totally different uses. The inclusion of a persulfate in the Saunders et al. work is to produce a polyacrylamide containing as little as possible of the monomeric compound, which is toxic. Alpenfels et al., on the other hand, are concerned entirely with the provision of certain structural features in electrophoresis gel equipment. The process disclosed in Alpenfels et al. is simply there as an example of a standard PAGE gel production process. There is no interest in Alpenfels for any type of process improvement, and no reason to add any sulfite, least of all certain amounts as shown in Saunders et al. Those skilled in the art of producing polyacrylamide gels would not look to Alpenfels et al. for any significant process information, and would not look to Saunders et al. for any useful information in connection with development of an electrophoresis gel process.

Furthermore, claim 1 now calls for the use of an uncoated plastic gel enclosure, which, as discussed above, is not effectively disclosed in Alpenfels et al.

In addition, the examiner's supposition that changing the Alpenfels et al. catalyst for a Saunders et al. catalyst would be expected to be obvious and matter little, lacks support. There is, indeed, all the reason in the world to expect that a change of catalyst, including a change of the active species, would have an effect. For example, in Hochstrasser et al. the use of sodium sulfite accelerated polymerization (col. 12 line 58). However, this catalyst also produced increased background staining. Accordingly, for the examiner to propose that a simple

substitution of catalyst used for production of one type of polyacrylamide product for catalyst used in a process for another product type, lacks a sound foundation.

Flesher et al., like Saunders et al., disclose a process for the production of linear polyacrylamides, for similar use as flocculants. The work of Flesher et al. is aimed at providing improved polyacrylamide flocculating agents that can be used in place of other such agents. Here again, cross-linking is undesirable (col. 2 lines 31-57). These polymers must be cationic for the intended uses (col. 3 lines 52-55), and are made so by the inclusion of a quaternary amine salt or a tertiary amine.

Flesher et al. contain no discussion of catalysts to be used in producing such polymers. The only mention of any catalysts is in the examples, and no reason is given why they were chosen or what if any advantage they provide.

As with Saunders et al., those skilled in the art would not look to this reference for any information useful in modifying the skimpy process information in Alpenfels et al., and would have no reason to substitute these redox catalysts for the ammonium persulfate/TEMED of Alpenfels et al.

In fact, combining Flesher et al. with Alpenfels et al. would be considered undesirable by those skilled in the art. Flesher et al. (col. 2 lines 50-57) advise conducting the reaction in the presence of a mercaptan to hold down the molecular weight of the polymer to a certain extent. The mercaptan used in the examples is 2-mercaptoethanol (Examples 5 and 6). However, as discussed previously in connection with the rejection over Ogawa et al., it is well known in the art that the presence of 2-mercaptoethanol is deleterious to gel formation. This item highlights the differences between the gel formation process of Alpenfels et al. (and the claimed process) and the linear polymer-flocculant process of Flesher et al.

Of the three references, only Alpenfels et al. discloses any information about prevention of oxygen from entering the polyacrylamide, and that reference discloses the use of an oxygen barrier coating. Nothing in the secondary references would cause one skilled in the art to substitute the redox catalysts of them for the catalyst of Alpenfels et al., and nothing would indicate that using an oxygen scavenger as claimed could obviate the need for the Alpenfels et al. oxygen barrier.

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PATENT

Withdrawal of this rejection is respectfully requested.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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